

REMARKS

Applicants would like to thank Examiner Kim and Primary Examiner Nolan for the guidance provided for overcoming the § 112, first paragraph rejection during the in person interview. The discussion during the interview focused on what the term “pretreatment” encompassed and suggestions for responding to the Office Action by defining the term or by amending the claims.

Applicants also would like to thank the Examiner for withdrawing the species election.

Status of the Claims

Claims 106-161 are currently pending in the present application. Claims 1-105 have been canceled without prejudice or disclaimer of the subject matter claimed therein. New claims 106-161 are directed to the same invention as claims 71-105. New claims 106-161 replace claims 71-105 and are reworded to describe the same invention. New claims 106-161 do not narrow the claimed subject matter originally presented.

Amendments to the Claims

New claims 106-161 do not introduce prohibited new matter. Support for the new claims is summarize in the table below

Claim	Representative Support
106	Claim 71; Example 1; Page 1, lines 8-10
107, 125, 143	Page 35, lines 24-26; Page 10, lines 16 and 17; Page 46, line 1
108, 126, 144	Claim 18; Page 12, lines 27 and 28; Page 46, lines 25 and 26
109, 127, 145	Claims 58 and 73
110, 128, 146	Claim 74

Claim	Representative Support
111, 129, 147	Claim 75
112, 130, 148	Claim 76
113, 131, 149	Claim 77
114, 132, 150	Claim 78
115, 133, 151	Claim 79
116, 134, 152	Claim 80
117, 135, 153	Claim 81
118, 136, 154	Claim 82
119, 137, 155	Claim 83; Page 53, lines 13, 14, and 21
120, 138, 156	Claim 84; Page 9, lines 24-26
121, 139, 157	Example 14
122, 140, 158	Page 7, line 26 to Page 8, line 2
123, 141, 159	Claim 85
124	Claim 86
142	Claim 94; Page 10, lines 12 and 13; Claim 18; Page 12, lines 27 and 28; Page 46, lines 25 and 26
160	Claim 105

Claim	Representative Support
161	Page 31, line 15; Example 12

Information Disclosure Statement

According to the Office Action, the foreign documents and non-patent literature listed on the Information Disclosure Statement (IDS) submitted on October 13, 2004 were not considered because the references were not available.

Applicants respectfully point out that according to MPEP 609 (I)(A)(2), documents submitted in a prior application need not be resubmitted in the present application under examination if the present application claims the benefit of the prior application under 35 U.S.C. § 120. The documents were previously submitted in the parent application, U.S. Application 09/257,188, now U.S. Patent 6,797,276.

For the convenience of the Patent Office, a clean copy of Form PTO-1449 is attached.

Priority Date of the Pending Claims

The Office Action alleges that the subject matter of claims 71 and 78-85 are accorded the priority date of February 25, 1999, the filing date of the parent application, U.S. Application 09/257,188. However, claims 72-77 and 86-105 are only accorded the priority date of the instant application.

Applicants respectfully point out that the present application is a continuation of parent application U.S. Application 09/257,188, filed on February 25, 1999. The present application is not a continuation-in-part of U.S. Application 09/257,188. Thus, the claims should all be accorded at a minimum the priority date of February 25, 1999. In fact, a review of the specification for U.S. Application 08/896,085, indicates that treating the skin with “penetration enhancers” is disclosed in 08/896,085. Accordingly, some of the claims should be accorded at a minimum the filing date of July 17, 1997.

Applicants also point out that claims 72-77 and 86-105 have been canceled and replaced with new claims 108-112 and 124-161. Claims 108-112 and 124-161 should not be deemed to

contain new matter because each of the claims is supported by the specification as originally filed. Support for the claims is summarized in the table above.

Rejection of the Claims Under 35 U.S. C. 112, Second Paragraph

Claims 71 and 86 are rejected under 35 U.S. C. 112, Second Paragraph, as being indefinite because the term “sufficient” is not defined by the claim.

Claims 71 and 86 have been replaced with new claims 106 and 124. New claims 106 and 124 do not contain the term “sufficient.”

Rejections of the Claims Under 35 U.S.C. § 112, First Paragraph

A. Claims 72-77 and 86-100 are rejected under 35 U.S.C. § 112, first paragraph because the specification does not contain a written description of the claimed invention.

Without acquiescing to the propriety of the rejection, claims 72-77 and 86-100 have been canceled and replaced with claims 108-112 and 124-148. Applicants point out that the following terms and phrases are described by the application as shown by their representative occurrences in the specification.

1. The phrase “disrupting only the outermost layer of said area of the skin” can be found in original claims 1 and 18; page 12, lines 27 and 28; and page 46, lines 25 and 26. (Applicants respectfully point out that although the phrase “outer surface of the skin,” is no longer used in the claims, the phrase is found on page 12, line 15.)
2. The phrase “at least one chemical” can be found in the specification in original claim 58.
3. The phrase “combinations thereof” can be found at page 4, line 22.
4. The phrase “emery board” can be found at claim 19 and throughout Example 5.
5. The term “concurrently” can be found on page 14 at lines 4-7 and 19.

B. Claims 71-105 are rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement for the scope of the claims.

The Office Action asserts that the specification enables a method for inducing an antigen specific immune response comprising pretreating with detergent and applying a formulation comprising a CT, LT, HA as an antigen and ADP-ribosylating exotoxin as an adjuvant, does not reasonably provide enablement for any method for inducing an antigen specific immune response comprising any formulation comprising any antigen, any adjuvant, and pretreating skin with any penetration enhancer, such as alcohol or device comprising tines.

New claim 106, which replaces claim 71, rewords claim 71 to include a definition for “pretreatment,” as suggested by Primary Examiner Nolan. Claim 106 includes the definition for pretreatment as “applying means for enhancing penetration and/or barrier disruption of the skin.” This definition does not in any way narrow the scope of the originally claimed subject matter.

The specification enables various methods of enhancing penetration and barrier disruption of the skin for pretreatment of the skin. Some representative examples of these enabled methods are shown in the Examples of the specification. For instance, alcohol swabbing is used in Examples 1 and 7; a depilatory is used in Example 3; a detergent is used in Example 2; a keratinolytic formulation is used in Example 4; abrasive pads such as emery boards are used in Example 5; and tape stripping is used in Example 16. These Examples show that these methods of pretreatment induce an antigen-specific immune response in a subject. As an example, Table 1 which summarizes the results of Example 1 show that pretreating the skin of mice with isopropanol (alcohol swabbing) increased the anti-CT titers in mice. Likewise, Tables 2a and 2b which summarizes the results of Example 2 show that pretreating the skin of mice with SDS (detergent) increased the anti-CT titer in mice. Tables 1, 2a, and 2b are representative examples of various methods of pretreating the skin that are enabled by the specification.

The Office Action alleges that the specification does not include alcohols as a source of penetration enhancer. As discussed above, Table 1 discloses that mice pretreated with isopropanol, an alcohol, have an increased anti-CT titer as compared to mice pretreated only with water.

The Office Action also alleges that the specification provides no working examples showing that pretreating a subject with a device comprising tines enhance the immune response. Applicants asserts that devices comprising tines are described in the specification and that mice pretreated with devices such as abrasive pads are shown in the Examples 5 and 6 to have an

increased anti-CT titer as compared to mice pretreated with only water. Although devices comprising tines are not identical to abrasive pads, one would expect them to have similar effects on the skin of mice, since they disrupt the outer surface of the skin. The Patent Office has not provided a reasonable explanation or evidence to doubt that a device comprising tines as a method of pretreatment for inducing an immune response.

Applicants respectfully point out that the initial burden is on the Patent Office to provide a reasonable explanation as to why the scope of protection provided by the claim is not adequately enabled by the disclosure. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Moreover, the court in *In re Marzocchi* stated that it is incumbent upon the Patent Office to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up its assertions with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The Office Action has not provided a reasonable explanation as to why the scope of the claims is not adequately enabled by the specification and has not provided evidence showing that the claims are not enabled by the specification.

Provisional Double Patenting Rejection

Claims 71-105 are provisionally rejected under the judicially created doctrine of double patenting over pending claims 1-11 of U.S. Patent No. 6,797,276 B1.

A terminal disclaimer is enclosed disclaiming the terminal part of the statutory term of any patent granted on application 10/790,715, which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. §§154, 156, 173, as presently shortened by any terminal disclaimer, of prior U.S. Patent 6,797,276. Accordingly, Applicants request withdrawal of the rejection.


Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this

application, they are invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
MORGAN, LEWIS & BOCKIUS LLP


Sally P. Teng
Registration No. 45,397

Date: **November 8, 2005**
Customer No. **009629**
Morgan, Lewis & Bockius LLP
1111 Pennsylvania Ave., N.W.
Washington, D.C. 20004
202.739.3000